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Analysis of Gender Differences in Peripheral Arterial Disease Prevalence from 1990 to 2019 in China

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【**Abstract**】 **Background** Peripheral artery disease（PAD）is a common and serious cardiovascular disease，which is prone to complications of limb ischemia and adverse cardiovascular events. There is a gender difference in the prevalence of PAD，which has been relatively poorly studied. A full understanding of gender differences in prevalence of PAD in China is essential for public health policy development. **Objective** To analyze the gender differences in the prevalence of PAD in China and their causes，providing a theoretical basis for targeted screening and preventive measures. **Methods** The number of PAD cases，prevalence，age-standardized prevalence，attributable risk factors for disease burden，and corresponding 95% uncertainty intervals（UI）were extracted from the 2019 Global Burden of Disease（GBD）database for males and females in China and females in Japan，Korea，India and globally. R language was used to analyze the data and visualize the analysis of this study. Joinpoint software was used to analyze the trend of PAD prevalence in males and females in China over time from 1990 to 2019，and the annual percentage change（APC）and average annual percentage change（AAPC）of PAD prevalence and their 95% confidence intervals（CI）were calculated. A Bayesian age-period-cohort（BAPC）model was used to predict the number and prevalence of PAD in 2020—2035. **Results** The estimated prevalence of PAD in China in 2019 was 71.74×100 000 for males and 213.15×100 000 for females. Compared with 1990，the number of PAD cases in 2019 increased by 154.22% in males and 181.27% in females. In 2019，the number of cases and prevalence of PAD among males in Japan，Korea，India and globally were all higher than those in 1990，but the age-standardized prevalence was lower. In 1990，the age-standardized prevalence of PAD among women in China was 57.80% and 76.35% of those in Japan and Korea，1.10 times and 1.33 times of those in Japan and Korea in 2019. The prevalence of PAD in Chinese men was 462.40/100 000 in 1990 and 989.79/100 000 in 2019，with an increase of 114.05%，and showed an upward trend during 1990 to 2019. The prevalence of PAD in Chinese women was 1 321.44 per 100 000 in 1990 and 3 055.85/100 000 in 2019，with an increase of 131.25%，and showed an upward trend from 1990 to 2019. The prevalence of PAD in Chinese women was 3.09 times higher than that of men in 2019. The age-

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standardized prevalence of PAD in Chinese males was 731.02/100 000 in 1990 and 744.96/100 000 in 2019，with an increase of 1.91%，showed an increasing trend from 1990 to 1993 and from 1993 to 2005，and a decreasing trend from 2005 to 2019. The age-standardized prevalence of PAD in Chinese women was 1 839.43/100 000 in 1990 and 2 022.13/100 000 in 2019，with an increase of 9.93%，showing an increasing trend from 1990 to 2005（P<0.05），and a non-significant trend from 2005 to 2009 and 2009 to 2019（P>0.05）. In 2019，the age-standardized prevalence of PAD in Chinese women was 2.71 times of men. BAPC model predicts that the number of PAD cases will reach 101.30×100，000 in Chinese men and 319.24×100 000 in Chinese women by 2035. In 2035，the number of Chinese women with PAD will increase by 49.77% compared with 2019. In terms of age，the largest number of Chinese women aged 65-69 with PAD in 2019 will be 35.15×100 000，and the largest number of women aged 70-74 with PAD in 2035 will be 55.89×100 000. In 2035，the number of Chinese women aged 40 to 44，45 to 49，50 to 54 and 55 to 59 with PAD will be lower than that in 2019，and the number of Chinese women aged 60 to 64，65 to 69，70 to 74，75 to 79，80 to 84，85 to 89，90 to 94 and ≥ 95 with PAD will be higher than that in 2019. In 2035，the age-standardized prevalence of PAD in Chinese men and women will be 712.09/100 000 and 1 945.97/100 000，respectively，decreasing by 4.41% and 3.77% compared with 2019. By age，the prevalence of PAD in Chinese women in 2035 will increase with age，and the prevalence of PAD in all age groups will be decreased compared with 2019 except for those aged ≥ 95 years. The disease burden of PAD in China in 2019 can be attributed to six risk factors，including hypertension，smoking，diabetes，renal insufficiency，high-salt diet and lead exposure. The most important risk factor for men was smoking（44.32%），followed by hypertension（18.97%）and diabetes（16.11%）. The most common risk factor for women was hypertension（32.31%），which was followed by diabetes（24.81%）and renal insufficiency（17.27%）. **Conclusion** The number of cases，prevalence and age-specific prevalence of PAD in Chinese women are significantly higher than those in men，and the age-standardized prevalence has already exceeded that of Japan and Korea. In the foreseeable future，the number of Chinese women suffering from PAD will further increase，and the number of elderly women suffering from PAD will increase more and more obviously. Therefore，more attention should be paid to the changes in gender and age，and gender differences in risk factors of PAD patients，and necessary screening and prevention measures should be taken.

【Key words】 Peripheral artery disease；Prevalence；Global burden of disease；Bayesian age-period-cohort；Bayesian forecast

Peripheral artery disease （PAD） has a high incidence and is the third most common cardiovascular disease

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after coronary artery disease and stroke[1]. Most patients with PAD are asymptomatic or have atypical symptoms, and only about 10% of patients have typical claudication symptoms, which poses a great challenge for the early diagnosis of PAD[2]. However, in patients with PAD, the incidence of adverse cardiovascular events and mortality is significantly increased, regardless of the presence of intermittent claudication, atypical leg pain, severe limb ischemia, etc[3-4].The risk of cardiovascular death in patients with PAD is increased by a factor of 3, and the more severe the disease is, the greater the likelihood that the patient will die from myocardial infarction or stroke[5-7].

The Global Burden of Disease （GBD） 2019 study estimates that there are approximately 113 million patients with PAD worldwide[8], and more than one-fifth will die from coronary or cerebrovascular disease within 10 years[9]. This is a considerable public health problem. However, compared with coronary artery disease and stroke, there is a lack of research on PAD, and public attention remains low, including clinical guidelines that rely on evidence from patients with coronary artery disease for risk management recommendations for patients with PAD[10]. The prevalence of PAD has been found to be gender-specific, with women accounting for 52.23% of PAD patients globally, especially in low- and middle-income countries, where the risk of peripheral arterial disease is higher in women than in men[2-3, 11]. Compared with men, women with PAD are at greater risk of reduced exercise capacity, reduced quality of life, risk of depression, and acute cardiovascular events[12-13]. At the same time, the increased burden of disability and mortality associated with PAD is more severe in women than in men[8]. Therefore, experts have called for more attention to be paid to gender differences in PAD patients and more attention to women with PAD[14-15].

Few studies have reported gender-related outcomes of PAD in China, therefore, a full understanding of the gender differences in the prevalence of PAD in China will help to develop prevention, diagnosis and control strategies more effectively.

1 Data and methods

1.1 Data sources The PAD prevalence data （1990-2019） required in this study were obtained from the 2019 GBD database （http://ghdx.healthdata.org/gbd-resultstool）. The data were extracted from the GBD database for men and women in China and women globally, Japan, Korea, and India, including the number of PAD prevalence, prevalence rate, age-standardized prevalence rate, attributable risk factors of disease burden, and the corresponding 95% uncertainty intervals （UIs）. R language （version 4.2.1） was used to analyze the data and visualize the analysis of this study.

1.2 Statistical methods

1.2.1 Joinpoint regression analysis Joinpoint software （version 4.9.1.0） was used to analyze the trend of

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PAD prevalence in Chinese men and women over time from 1990-2019. The Monte Carlo permutation test was the default preferred model screening method of Joinpoint software and corrected for the level of statistical significance, with $P<0.05$ considered significant[16-17]. The number of joinpoints is related to the number of study observations （i.e., the time span of the data）, and the system defaults to a minimum of 0 and a maximum of 5, which can be defined by the researcher according to the needs[16]. In this paper, the number of connection points was set to 2. The annual percent change （APC） and average annual percent change （AAPC） of PAD prevalence and its 95% credible interval （CI） were calculated.

1.2.2 Bayesian age-periodcohort （BAPC） model This study used the BAPC model to predict the number and prevalence of PAD in 2020-2035 based on the number and prevalence of PAD in 1990-2019 in the GBD database. The GBD dataset provides data on the prevalence of PAD in people ≥40 years of age, and the population was divided into 12 age groups of 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, and ≥95 years of age with a 5-year age range. The BAPC model was fitted using a Poisson model in integrated nested Laplace approximation （INLA） for predicting trends in disease epidemiology[18]. In this study, second-order random walk （RW2） modeling[19] was used to study the age, period, and cohort effects to estimate the number of people and prevalence of PAD, and this prediction process was implemented through the BAPC and INLA packages in the R language.

2 Results

2.1 Prevalence of PAD among men and women in China, Japan, Korea, India and the world in 1990 and 2019 The prevalence of PAD in China in 2019 was 71.74×100,000 for men and 213.15×100,000 for women. Compared with 1990, the number of PAD cases in 2019 increased by 154.22% for men and 181.27% for women, as shown in table 1.

Table 1 Prevalence of PAD among Chinese men and women in China，Japan，Korea，India and globally in 1990 and 2019

Area	Gender	Number of patients			Crude prevalence			Age-standardized prevalence		
		1990（95%）（×100,000）	2019（95%）（×100,000）	Rate of change（%）	1990（95%）（1/100,000）	2019（95%）（1/100,000）	Rate of change（%）	1990（95%）（1/100,000）	2019（95%）（1/100,000）	Rate of change
China	Male	28.22（24.03，32.53）	71.74（61.29，82.49）	154.22	462.40（393.73，533.09）	989.79（845.60，1 138.07）	114.05	731.02（631.44，836.51）	744.96（644.62，850.82）	1.91

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	Female	75.78 (65.04, 86.78)	213.15 (183.34, 244.52)	181.27	1 321.44 (1 134.16, 1 513.18)	3 055.85 (2 628.40, 3 505.48)	131.25	1 839.43 (1 593.06, 2 095.46)	2 022.13 (1 750.00, 2 309.13)	9.93
Japan	Female	30.72 (26.73, 34.70)	37.26 (32.11, 42.65)	21.29	4 801.14 (4 177.38, 5 422.56)	5 686.97 (4 901.04, 6 509.51)	18.45	3 182.64 (2 782.59, 3 587.70)	1 846.52 (1 606.47, 2 091.10)	-41.98
Korea	Female	3.88 (3.34, 4.42)	7.53 (6.51, 8.61)	94.07	1 756.55 (1 512.74, 2 001.33)	2 850.98 (2 466.53, 3 260.43)	62.31	2 409.29 (2 083.25, 2 739.95)	1 519.64 (1 314.65, 1 737.66)	-36.93
India	Female	21.43 (18.33, 24.63)	61.15 (52.96, 70.11)	185.35	522.29 (446.86, 600.39)	902.56 (781.69, 1 034.75)	72.81	1 135.33 (985.40, 1 300.95)	1 105.89 (959.02, 1 261.32)	-2.59
Global	Female	447.95 (390.62, 507.73)	760.93 (665.87, 861.71)	69.87	1 686.50 (1 470.66, 1 911.55)	1 973.12 (1 726.63, 2 234.45)	16.99	2 181.02 (1 905.72, 2 471.79)	1 735.06 (1 519.05, 1 964.04)	-20.45

In 2019, the number and prevalence of female PAD in Japan, Korea, India, and globally increased compared with 1990, but the age-standardized prevalence decreased. Among them, the largest decrease was 41.98% in Japanese women, 36.93% in Korea, 2.59% in India, and 20.45% globally. However, the age-standardized prevalence of PAD in Chinese females increased by 9.93%. In 1990, the age-standardized prevalence of PAD in Chinese females was 57.80% and 76.35% of that in Japanese and Korean females, respectively, and in 2019 it will be 1.10 times and 1.33 times of that in Japanese and Korean females, respectively. In 1990, the number of women with PAD in China accounted for 16.92% of the global population, and in 2019, it will account for 28.01% of the global population.

2.2 Joinpoint regression analysis of changes in crude and age-standardized prevalence rates of PAD in China

The crude prevalence rate of male PAD in China was 462.40 per 100,000 in 1990 and 989.79 per 100,000 in 2019, with an increase of 114.05%, as shown in table 1 and figure 1. The crude prevalence rate of male PAD in China was 462.40/10,000 in 1990 and 989.79/10,000 in 2019, with an increase of 114.05%, as shown in table 1 and figure 2. The APCs of 1990-1999, 1999-2007, and 2007-2019 showed an increasing trend, with the APCs of 2.58%, 3.17%, and 2.39%, respectively. The AAPC was 2.66% from 1990 to 2019, as shown in table 2. The crude prevalence rate of female PAD was 1,321.44/10,000 in 1990 and 3,055.85/10,000 in 2019, with an increase of 131.25%, as shown in table 1 and figure 2. The years 1990-2006, 2006-2009, 2009-2019 showed an increasing trend, with APCs of 2.90%, 2.21% and 3.24% respectively, and the AAPC for 1990-2019 was 2.94%, as shown in table 2.

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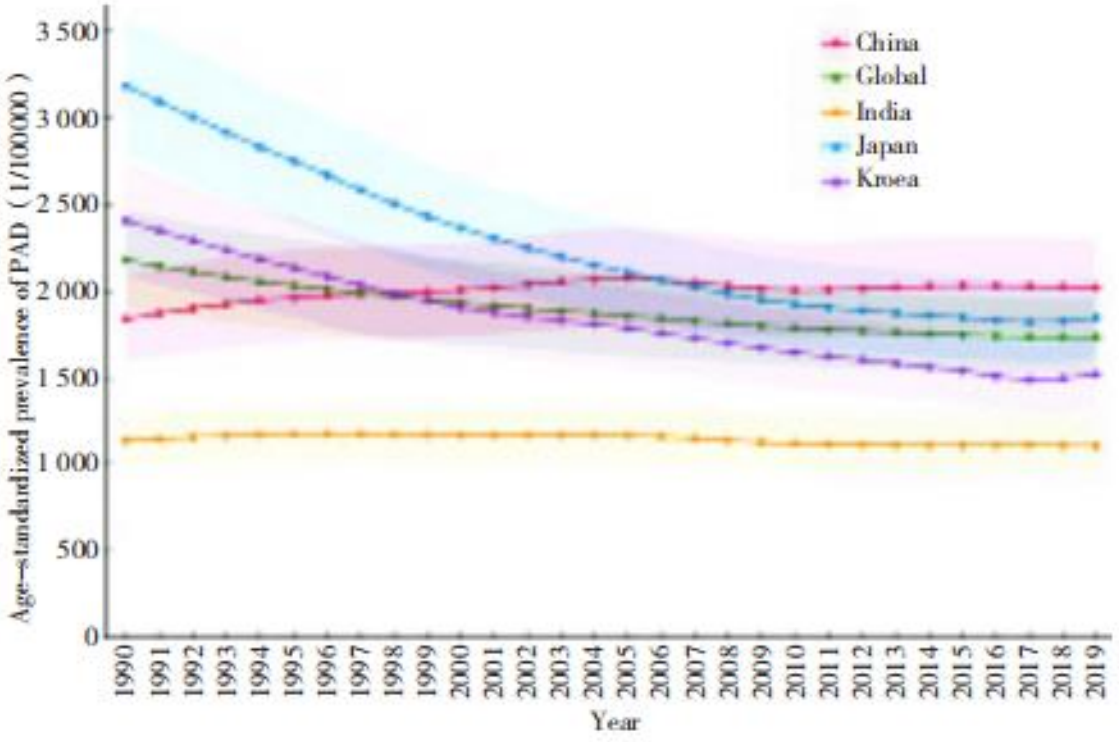

Note: PAD = peripheral arterial disease

Figure 1 Trends in the age-standardized prevalence of PAD in women from 1990 to 2019 in globally，China，India，Japan，and Korea

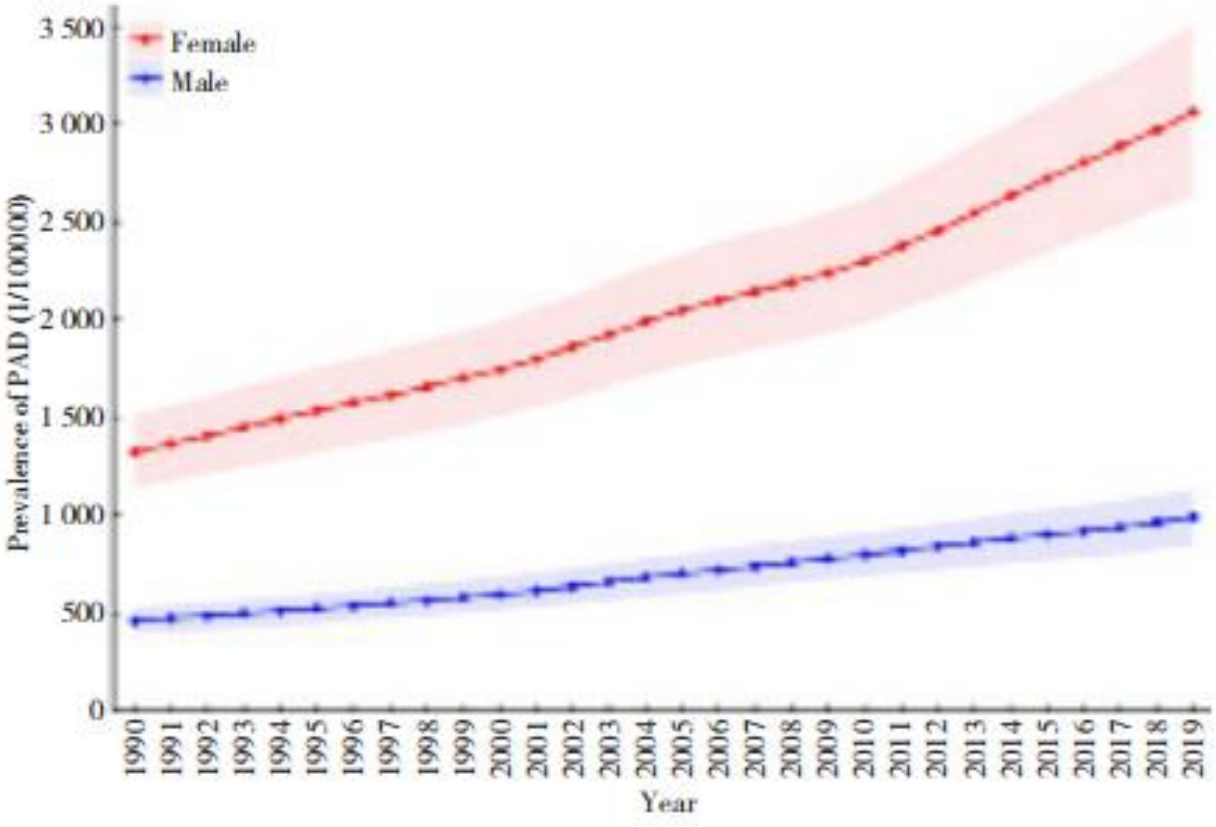

Figure 2 Gender prevalence of PAD in China from 1990 to 2019

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Table 2 Temporal changes of PAD prevalence and age-standardized prevalence in China from 1990 to 2019

Item	Gender	Trend 1		Trend 2		Trend 3		AAPC (95%*CI*)
		Year	(95%*CI*)	Year	(95%*CI*)	Year	APC (95%*CI*)	
Crude prevalence	Male	1990—1999	2.58 (2.52, 2.65)	1999—2007	3.17 (3.07, 3.26)	2007—2019	2.39 (2.34, 2.43)	2.66 (2.63, 2.70)
	Female	1990—2006	2.90 (2.84, 2.96)	2006—2009	2.21 (0.67, 3.77)	2009—2019	3.24 (3.11, 3.36)	2.94 (2.78, 3.10)
Age-standardized prevalence	Male	1990—1993	0.91 (0.68, 1.14)	1993—2005	0.49 (0.46, 0.52)	2005—2019	-0.50 (-0.52, -0.48)	0.05 (0.03, 0.08)
	Female	1990—2005	0.73 (0.65, 0.81)	2005—2009	-0.93 (-1.87, 0.03)	2009—2019	0.10 (-0.05, 0.25)	0.28 (0.14, 0.42)

The age-standardized prevalence rate of male PAD in China was 731.02 per 100,000 in 1990 and 744.96 per 100,000 in 2019, with an increase of 1.91%, as shown in table 1 and figure 3. The increasing trend was observed in 1990-1993 and 1993-2005, with an APC of 0.91%. The age-standardized prevalence rate of PAD in Chinese women was 1,839.43 per 100,000 in 1990 and 2,022.13 per 100,000 in 2019, with an increase of 9.93%. The age-standardized prevalence rate of PAD in Chinese women was 1,839.43 per 100,000 in 1990 and 2,022.13 per 100,000 in 2019, with an increase of 9.93%, as shown in table 1 and figure 3. There was an upward trend in 1990-2005, with an AAPC of 0.73%, and the change trends in the years 2005-2009 and 2009-2019 were not significant (*P*>0.05). The AAPC for 1990-2019 was 0.28, see Table 2.

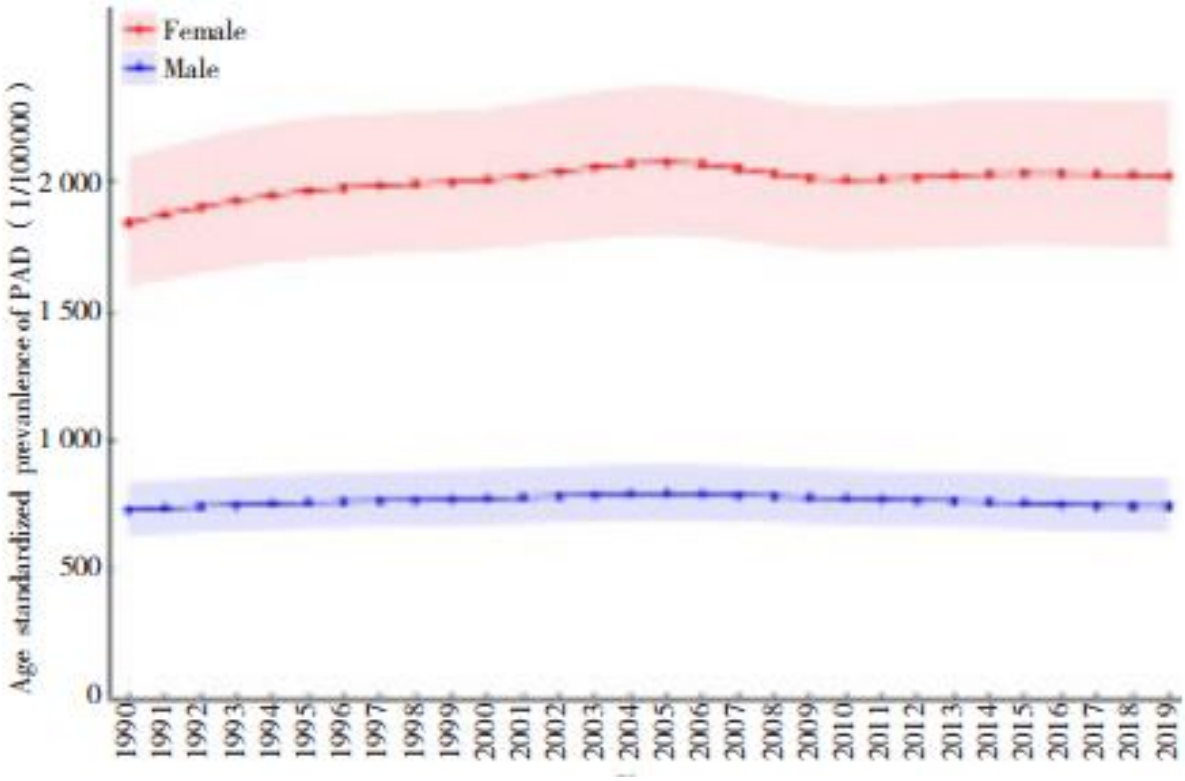

Figure 3 Gender and age standardized prevalence of PAD in China from 1990 to 2019

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2.3 Trend prediction of PAD in China in 2035 The BAPC model predicts that in 2035, the number of male PAD patients in China will reach 101.30×100,000, and the number of female PAD patients will reach 3,192.4×100,000, and the number of female PAD patients in 2035 will increase by 49.77% compared with that in 2019. By age, the number of Chinese women aged 65-69 with PAD will be the highest in 2019, at 35.15×100,000, and the number of women aged 70-74 will be the highest in 2035, at 55.89×100,000. In 2035, the number of Chinese women aged 40-44, 45-49, 50-54, and 55-59 with PAD will be lower than that in 2019, and the number of women aged 60-64, 65-69, 70-74, and 75-59 will be lower than that in 2019, and the number of women aged 60-64, 65-69, 70-74, and 75-59 will be lower than that in 2019. ~In 2035, the number of Chinese women aged 40-44, 45-49, 50-54, and 55-59 years with PAD will be lower than that in 2019, while the number of those aged 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, and ≥95 years will be higher than that in 2019, as shown in table 3 and figure 4A.

Table 3 Comparison of number of cases and age-standardized prevalence of PAD in China in 2019 and 2035

Stratification	Number of patients			Age-standardized prevalence rate/age-stratified prevalence rate		
	2019（×100000）	2035（×100000）	rate of change（%）	2019（×100000）	2035（1/100000）	rate of change（%）
Male	71.74（61.29，82.49）	101.30（74.17，128.43）	41.20	744.96（644.62，850.82）	712.09（521.26，902.92）	-4.41
Female	213.15（183.34，244.52）	319.24（211.74，426.74）	49.77	2 022.13（1 750.00，2 309.13）	1 945.97（1 290.41，2 601.54）	-3.77
Age						
40~44	3.53（2.63，4.53）	3.44（2.03，4.86）	-2.55	709.33（528.11，909.28）	685.46（451.91，997.17）	-3.37
45~49	10.28（8.00，13.02）	10.23（6.48，13.98）	-0.49	1 727.05（1 343.83，2 186.38）	1 669.34（1 141.36，2 356.88）	-3.34
50~54	20.45（15.47，26.47）	16.84（10.99，22.68）	-17.65	3 283.85（2 484.01，4 250.95）	3 176.14（2 211.35，4 416.94）	-3.28
55~59	24.22（18.92，29.50）	23.60（15.55，31.65）	-2.56	5 130.90（4 009.67，6 250.79）	4 954.32（3 467.83，6 858.72）	-3.44
60~64	28.05（21.86，34.20）	37.79（24.90，50.67）	34.72	7 174.76（5 591.51，8 748.45）	6 911.64（4 838.26，9 567.32）	-3.67
65~69	35.15（28.53，42.76）	54.23（35.74，72.71）	54.28	9 808.05（7 962.41，11 931.32）	9 534.03（6 674.27，13 197.34）	-2.79
70~74	31.48（24.75，38.93）	55.89（36.84，74.94）	77.54	12 834.99（10 090.64，15 872.26）	12 644.82（8 851.97，17 502.76）	-1.48
75~79	24.68（19.95，29.94）	47.23（31.13，63.32）	91.37	15 710.38（12 701.39，19 056.28）	15 578.80（10 906.09，21 564.03）	-0.84
80~84	19.50（15.94，23.57）	42.34（27.91，56.77）	117.10	18 233.42（14 904.87，22 040.04）	18 047.91（12 634.59，24 981.53）	-1.02
85~89	11.03（9.15，13.23）	22.05（14.54，29.57）	99.91	19 956.90（16 549.96，23 939.22）	19 644.12（13 752.07，27 191.05）	-1.57
90~94	3.90（3.26，4.62）	8.00（5.28，10.73）	105.10	21 005.15（17 575.78，24 849.58）	20 503.84（14 353.82，28 381.23）	-2.39
≥95	0.89（0.74，1.06）	2.42（1.59，3.24）	171.90	19 900.02（16 381.60，23 738.57）	21 118.14（14 783.68，29 231.74）	6.12

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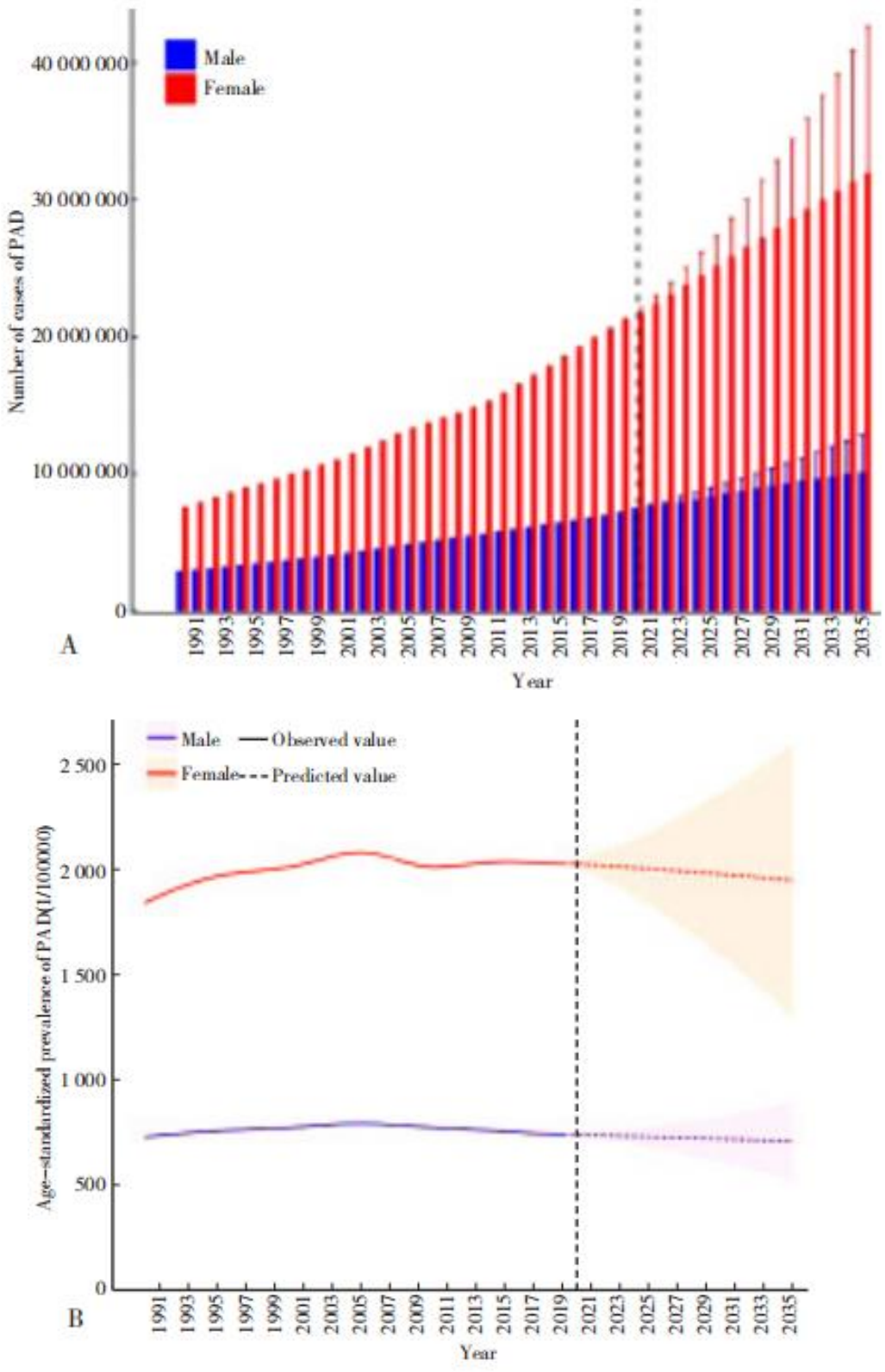

Note: A is the prediction of the number of patients and B is the prevalence of age

Figure 4 Prediction of the changing trend of the number cases and age-standardized prevalence of PAD by gender in China from 2020 to 2035

In 2035, the age-standardized prevalence of PAD in China will be 712.09/100,000 for men and 1945.97/100,000 for women, a decrease of 4.41% and 3.77%, respectively, compared with 2019. According to age-specific statistics, in 2035, the prevalence of PAD in Chinese women of all age strata increased with age, and except for those ≥95 years of age, the prevalence of all other age groups decreased compared with that in 2019, as shown in table 3 and figure 4B.

2.4 Risk factor analysis for attributing the disease burden of PAD in China The disease burden of PAD in China in 2019 could be attributed to 6 risk factors, namely hypertension, smoking, diabetes mellitus, renal insufficiency, high salt diet, and lead exposure. The most important risk factor for men was smoking （44.32%）, followed by hypertension （18.97%） and diabetes （16.11%）. In females, the most important risk factor was hypertension （32.31%）, followed by diabetes mellitus （24.81%） and renal insufficiency （17.27%）, and smoking only accounted for 14.91%, as shown in table 4.

Table 4 Proportion of risk factors of PAD disease burden in China in 2019

Risk factors	Female	Male
Hypertension	32.31	18.97
Diabetes	24.81	16.11
Kidney Insufficiency	17.27	10.66
Smoking	14.91	44.32
High Salt Diet	8.40	7.81
Lead exposure	2.30	2.13

3 Discussion

This study used GBD 2019 data to assess the prevalence of PAD in China from 1990-2019, and found that the number of PAD patients, prevalence rate, and age-standardized prevalence rate in China increased from 1990-2019. In 2019, the number of PAD patients in China amounted to more than 28 million, with the number of female patients being more than 21 million. In 2019, the number of PAD patients in China will reach more than 28 million, of which more than 21 million will be women. In 2019, the number of PAD patients in China will reach more than 28 million,

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of which more than 21 million will be women. It is expected that by 2035, the number of women with PAD in China will reach 32 million, which is 3.15 times higher than that of men. Although asymptomatic PAD accounts for more than 50% of these patients, and lower extremity function and quality of life are not significantly affected, it is in fact a symptom of poor overall vascular health and a predictor of potentially fatal cardiovascular events in the future.

Patients with asymptomatic PAD have a 20%-60% increased risk of myocardial infarction and a 40% increased risk of stroke[7, 20]. PAD implies a higher incidence of multivessel disease, which is a huge medical and economic burden worldwide. Therefore, understanding the prevalence characteristics of PAD can better guide disease prevention and treatment, as well as public health policy development.

In previous studies on PAD, men had been considered as an independent risk factor for PAD due to gender bias in sampling in population screening or clinical studies and gender differences in treatment-seeking behavior[14, 21-23]. However, the current understanding of gender differences in PAD has changed with the increased research on gender in PAD in recent years. Data in recent years suggest that the prevalence of PAD is higher in women[24]. A cross-sectional study in an urban population in Beijing also found that the prevalence of PAD was higher in women than in men, with 8.0% in men and 13.6% in women[25]. The present study also found that the prevalence of PAD in Chinese women was significantly higher than that in men.

Studies have shown that asymptomatic and atypical symptoms are more common in women with PAD, and atypical symptoms in women are often misdiagnosed as arthritis, spinal stenosis, or neuropathy[15]. However, because leg strength and cardiorespiratory fitness are lower in women compared to men, women experience greater impairment in lower extremity function and strength and greater loss of quality of life when PAD disease severity is similar[26-27].

Previous studies have seldom analyzed the reasons for the higher prevalence of PAD in women than in men, and the mechanisms are unclear and may be multifactorial, related to differences in socio-demographic structure, diagnostic methods and risk factors.

Firstly, analyzing the socio-demographic structure, the life expectancy of the Chinese population has been increasing over the past 30 years, and the average life expectancy of females is longer than that of males, with females accounting for 54.39% of the population aged 70 years or older, and females accounting for 61.09% of the population aged 80 years or older[28]. The prevalence of PAD increases with age. In this study, we found that the prevalence of PAD in Chinese females aged 75 years or older was more than 15%, and the global population, including China, is aging rapidly, which is also confirmed by the prediction of PAD prevalence in China in 2035, and in 2035, the number

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of PAD patients in China will increase further, while the age-standardized prevalence rate will decrease, which is exactly a manifestation of the aging of the population. This may be one of the reasons for the gender differences in PAD prevalence[23, 29]. In addition, the mortality rate of PAD in Chinese men has been increasing over the past 30 years, whereas the mortality rate of PAD in women has been decreasing and their survival time has been further prolonged[30]. Some studies have also attributed this to the possible survival advantage of women in coronary heart disease and stroke. Because patients with PAD rarely die from PAD itself, and most die from other cardiovascular diseases, whereas men are more likely to die from coronary heart disease [30-31], women with PAD have a survival advantage over men. These may be another reason for the increasing prevalence of PAD in women.

The second is the diagnostic method for PAD. The ankle brachial index（ABI） is a non-invasive tool for screening and diagnosis of PAD, and the 2016 American Heart Association/American College of Cardiology （AHA/ACC） guidelines recommend the ABI as the initial diagnostic method for patients with PAD, and patients with an ABI of <0.90 can be diagnosed with PAD[2]. The ABI varies among different sexes. The ABI varies between genders. In a Scottish screening of adults with no history of cardiovascular disease, the mean ABI was 0.05 lower in women than in men （1.01 for women and 1.06 for men） [32]. An epidemiologic study in the United States, which was sex- and race-specific, showed that the ABI was approximately 0.02 lower in women than in men[33]. And this difference may be related to normal physiological differences between genders such as height and diameter of small blood vessels in the limbs. Studies have shown that the higher the height, the higher the systolic blood pressure at the ankle and the higher the ABI value. Usually, the average height of men is higher than that of women, so the average ABI of men is higher than that of women[34-35]. In view of this, some scholars have suggested that using ABI<0.90 as the standardized criterion for diagnosing PAD between men and women may not be able to accurately differentiate the actual prevalence of PAD between different genders[11]. In China, the difference in height between genders may be more obvious, and epidemiologic studies are needed to prove whether this may lead to a greater gender difference in ABI. On the other hand, the prevalence of PAD in men may be underestimated. Some patients with post-exercise claudication will have a normal resting ABI, so exercise ABI testing can help to differentiate whether PAD is present[5], but detecting post-exercise ABI is usually not feasible in large epidemiologic studies[11]; the prevalence of severe limb ischemia and amputation is higher in males[36-37], whereas patients with pre-existing amputation or severe limb ischemia have usually been excluded from population-based studies; PAD in men is more common in those with lower socioeconomic status as well as education, which may be associated with risk factors such as smoking or unhealthy dietary patterns[11, 38-40]. Screening for ABI in China is more common in large medical centers and urban

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communities in the east, and less common in economically underdeveloped areas and rural grassroots in the central and western parts of the country[41-43]. These may all contribute to the underestimation of PAD in men. Then for the differences in risk factors. In this study, we analyzed the risk factors attributable to the burden of disease for PAD in China in 2019. For men, smoking was the most important risk factor, accounting for 44.32%. For women, hypertension was the most important risk factor, followed by diabetes mellitus, and smoking was only the fourth risk factor for women. Although the prevalence of smoking is lower in women than in men, the risk of exposure to secondhand smoke is significantly higher[9], and it is estimated that more than half of female nonsmokers in China are exposed to passive smoking [44-45], which may be a potential reason for the increased prevalence of PAD in women[30-31]. In addition, diabetes mellitus is the second risk factor for the disease burden of PAD in women, and studies have shown that women with diabetes mellitus have a higher risk of developing PAD than men[24, 29]. In addition to this, women have their own risk factors, such as estrogen-related changes in the postmenopausal state, higher serum levels of oxidative stress markers in women [46], and the use of oral contraceptives. It has been suggested that one of the plausible explanations for the higher prevalence of PAD in women than in men under the age of 40 may be the use of oral contraceptives[47]. Women who experience complications during pregnancy such as pre-eclampsia and hypertensive syndrome of pregnancy are at higher risk of developing PAD [48-49].

In summary, the prevalence of PAD in Chinese women is significantly higher than that in men due to gender differences in socio-demographic structure, diagnostic methods and risk factors. Meanwhile, this study also found that the age-standardized prevalence of PAD among Chinese women has increased significantly over the past 30 years, and has even surpassed that of high-income countries such as Japan and South Korea, and far surpassed that of India, which is also a developing country. In contrast, the age-standardized prevalence of female PAD in Japan, South Korea, India, and globally has decreased over the same period, and the age-standardized prevalence of male PAD in China has also declined over the past decade. More importantly, Chinese female PAD patients accounted for approximately 28.01% of global female PAD patients in 2019. The present study predicted that the number of female PAD patients in China would increase by about 49.77% by 2035 compared with the number of female PAD patients in 2019. In the foreseeable future, as the population grows, the number of female PAD patients in China will increase by approximately 49.77% compared with 2019. Therefore PAD is a health problem that cannot be ignored, and awareness of the disease among medical practitioners and the general public should be strengthened. In particular, more gender-based epidemiologic and clinical studies are needed to improve the prevention, early diagnosis, and treatment of PAD, especially in women, in order to reduce the economic burden and negative consequences associated

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with PAD.

This study has the following limitations: firstly, the data provided by the GBD depend greatly on the quality and quantity of data used during modeling, and the quality and extent of missing data vary greatly between countries and regions, which may bias the estimation of the burden of PAD [50]. Secondly, PAD is often accompanied by other serious coexisting diseases such as myocardial infarction or stroke, which may mask the harm caused by PAD itself and lead to underestimation of the burden of PAD. Thirdly, the lack of data in the GBD database attributable to other risk factors, such as hypercholesterolemia, limits the ability of this study to comprehensively analyze the overall risk factors and burden.

Authors' contributions: Liu Linbo and Shi Sen were responsible for the overall design and review of the paper; Liu Linbo, Liao Zhijie, and Yang Wenfan were responsible for the data analysis, interpretation of the data, and review of the literature; Yang Wenfan, Bai Dandan, and Wang Dongmei were responsible for the drawing of the paper's images, organizing, and drafting the paper; and Shi Sen was responsible for the paper's revisions and proofreading. All authors jointly determined the final version of the paper.

There is no conflict of interest in this paper.

Reference

［1］BENJAMIN E J，BLAHA M J，CHIUVE S E，et al. Heart disease and stroke statistics-2017 update：a report from the American Heart Association［J］. Circulation，2017，135（10）：e146-603. DOI：10.1161/CIR.0000000000000485.

［2］GERHARD-HERMAN M D，GORNIK H L，BARRETT C，et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease：a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines［J］. Circulation，2017，135（12）：e726-779. DOI：10.1161/CIR.0000000000000471.

［3］SONG P G，RUDAN D A，ZHU Y J，et al. Global，regional，and national prevalence and risk factors for peripheral artery disease in 2015：an updated systematic review and analysis［J］. Lancet Glob Health，2019，7（8）：e1020-1030. DOI：10.1016/S2214-109X（19）30255-4.

［4］CRIQUI M H，ABOYANS V. Epidemiology of peripheral artery disease［J］. Circ Res，2015，116（9）：1509-1526. DOI：10.1161/CIRCRESAHA.116.303849.

［5］FOLEY T R，ARMSTRONG E J，WALDO S W. Contemporary evaluation and management of lower extremity peripheral artery disease［J］. Heart，2016，102（18）：1436-1441. DOI：10.1136/heartjnl-2015-309076.

chinaXiv:202310.03350v1

［6］AGRAWAL K，EBERHARDT R T. Contemporary medical management of peripheral arterial disease：a focus on risk reduction and symptom relief for intermittent claudication［J］. Cardiol Clin，2015，33（1）：111-137. DOI：10.1016/j.ccl.2014.09.010.

［7］CONTE S M，VALE P R. Peripheral arterial disease［J］. Heart Lung Circ，2018，27（4）：427-432. DOI：10.1016/j.hlc.2017.10.014.

［8］LIN J F，CHEN Y B，JIANG N，et al. Burden of peripheral artery disease and its attributable risk factors in 204 countries and territories from 1990 to 2019［J］. Front Cardiovasc Med，2022，9：868370. DOI：10.3389/fcvm.2022.868370.

［9］FOWKES F G，RUDAN，RUDAN I，et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010：a systematic review and analysis［J］. Lancet，2013，382（9901）：1329-1340. DOI：10.1016/S0140-6736（13）61249-0.

［10］TAKAHARA M，IIDA O，KOHSAKA S，et al. Diabetes mellitus and other cardiovascular risk factors in lower-extremity peripheral artery disease versus coronary artery disease：an analysis of 1，121，359 cases from the nationwide databases［J］. Cardiovasc Diabetol，2019，18（1）：155. DOI：10.1186/s12933-019-0955-5.

［11］FOWKES F G，ABOYANS V，FOWKES F J，et al. Peripheral artery disease：epidemiology and global perspectives［J］. Nat Rev Cardiol，2017，14（3）：156-170. DOI：10.1038/nrcardio.2016.179.

［12］JELANI Q U，MENA-HURTADO C，BURG M，et al. Relationship between depressive symptoms and health status in peripheral artery disease：role of sex differences［J］. J Am Heart Assoc，2020，9（16）：e014583. DOI：10.1161/JAHA.119.014583.

［13］BROSTOW D P，PETRIK M L，STAROSTA A J，et al. Depression in patients with peripheral arterial disease：a systematic review［J］. Eur J Cardiovasc Nurs，2017，16（3）：181-193. DOI：10.1177/1474515116687222.

［14］POLLAK A W. PAD in women：the ischemic continuum［J］. Curr Atheroscler Rep，2015，17（6）：513. DOI：10.1007/s11883-015-0513-x.

［15］HIRSCH A T，ALLISON M A，GOMES A S，et al. A call to action：women and peripheral artery disease：a scientific statement from the American Heart Association［J］. Circulation，2012，125（11）：1449-1472. DOI：10.1161/CIR.0b013e31824c39ba.

［16］LI H Z，DU L B. Application of joinpoint regression models to the analysis of time trends in tumor epidemiology［J］. Chinese Journal of Preventive Medicine，2020，54（8）：908-912. DOI：10.3760/cma.j.cn112150-20200616-00889.

chinaXiv:202310.03350v1

［17］WANG H X，FAN W L，YANG X Y，et al. Protein-energy malnutrition incidence in China：trend in 1990-2019 and future trend in 2020-2029［J］. Chinese General Practice，2023，26（5）：591-597.

［18］XU Q Q，YAN Y F，CHEN H，et al. A study on the prediction of the realization of the sustainable development goals for the mortality rate of the four major chronic diseases in China［J］. Chinese Journal of Epidemiology，2022，43（6）：878-884. DOI：10.3760/cma.j.cn112338-20211028-00830.

［19］LIANG S S，ZHOU Z H，LI C C，et al. Diabetes in China：burden analysis between 1990 and 2019 and incidence prediction between 2020 and 2030［J］. Chinese General Practice，2023，26（16）：2013-2019.

［20］ANDERSON J L，HALPERIN J L，ALBERT N M，et al. Management of patients with peripheral artery disease（compilation of 2005 and 2011 ACCF/AHA guideline recommendations）：a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines［J］. Circulation，2013，127（13）：1425-1443. DOI：10.1161/CIR.0b013e31828b82aa.

［21］TEODORESCU V J，VAVRA A K，KIBBE M R. Peripheral arterial disease in women［J］. J Vasc Surg，2013，57（4）：18S-26S. DOI：10.1016/j.jvs.2012.10.115.

［22］GRENON S M，COHEN B E，SMOLDEREN K，et al. Peripheral arterial disease，gender，and depression in the Heart and Soul Study［J］. J Vasc Surg，2014，60（2）：396-403. DOI：10.1016/j.jvs.2014.02.013.

［23］CHASE-VILCHEZ A Z，CHAN I H Y，PETERS S A E，et al. Diabetes as a risk factor for incident peripheral arterial disease in women compared to men：a systematic review and metaanalysis［J］. Cardiovasc Diabetol，2020，19（1）：151. DOI：10.1186/s12933-020-01130-4.

［24］SRIVARATHARAJAH K，ABRAMSON B L. Women and peripheral arterial disease：a review of sex differences in epidemiology，clinical manifestations，and outcomes［J］. Can J Cardiol，2018，34（4）：356-361. DOI：10.1016/j.cjca.2018.01.009.

［25］HE Y，JIANG Y，WANG J，et al. Prevalence of peripheral arterial disease and its association with smoking in a population-based study in Beijing，China［J］. J Vasc Surg，2006，44（2）：333-338. DOI：10.1016/j.jvs.2006.03.032.

［26］MORRISON A，ADAY A W. Sex as a key determinant of peripheral artery disease：epidemiology，differential outcomes，and proposed biological mechanisms［J］. Can J Cardiol，2022，38（5）：601-611. DOI：10.1016/j.cjca.2022.02.021.

［27］MCDERMOTT M M，FERRUCCI L，LIU K，et al. Women with peripheral arterial disease experience faster functional decline than men with peripheral arterial disease［J］. J Am Coll Cardiol，2011，57（6）：707-714.

chinaXiv:202310.03350v1

DOI：10.1016/j.jacc.2010.09.042.

［28］XIANG X，WANG Y. Current situation, characteristics, causes and countermeasures of population ageing in China[J]. Chinese Journal of Gerontology，2021，41（18）：4149-4152. DOI：10.3969/j.issn.1005-9202.2021.18.072.

［29］PATEL T，BAYDOUN H，PATEL N K，et al. Peripheral arterial disease in women：the gender effect［J］. Cardiovasc Revasc Med，2020，21（3）：404-408. DOI：10.1016/j.carrev.2019.05.026.

［30］GONG W，SHEN S H，SHI X J. Secular trends in the epidemiologic patterns of peripheral artery disease and risk factors in China from 1990 to 2019：findings from the global burden of disease study 2019［J］. Front Cardiovasc Med，2022，9：973592. DOI：10.3389/fcvm.2022.973592.

［31］SAMPSON U K，FOWKES F G，MCDERMOTT M M，et al. Global and regional burden of death and disability from peripheral artery disease：21 world regions，1990 to 2010［J］. Glob Heart，2014，9（1）：145-158.e21. DOI：10.1016/j.gheart.2013.12.008.

［32］PRICE J F，STEWART M C，DOUGLAS A F，et al. Frequency of a low ankle brachial index in the general population by age，sex and deprivation：cross-sectional survey of 28，980 men and women［J］. Eur J Cardiovasc Prev Rehabil，2008，15（3）：370-375. DOI：10.1097/HJR.0b013e3282f8b36a.

［33］ABOYANS V，CRIQUI M H，MCCLELLAND R L，et al. Intrinsic contribution of gender and ethnicity to normal ankle-brachial index values：the Multi-Ethnic Study of Atherosclerosis（MESA）［J］. J Vasc Surg，2007，45（2）：319-327. DOI：10.1016/j.jvs.2006.10.032.

［34］ISHIDA A，MIYAGI M，KINJO K，et al. Age- and sex-related effects on ankle-brachial index in a screened cohort of Japanese：the Okinawa Peripheral Arterial Disease Study（OPADS）［J］. Eur J Prev Cardiol，2014，21（6）：712-718. DOI：10.1177/2047487312462822.

［35］KAPOOR R，AYERS C，VISOTCKY A，et al. Association of sex and height with a lower ankle brachial index in the general population［J］. Vasc Med，2018，23（6）：534-540. DOI：10.1177/1358863X18774845.

［36］LO R C，BENSLEY R P，DAHLBERG S E，et al. Presentation，treatment，and outcome differences between men and women undergoing revascularization or amputation for lower extremity peripheral arterial disease［J］. J Vasc Surg，2014，59（2）：409-418.e3. DOI：10.1016/j.jvs.2013.07.114.

［37］WALTER N，ALT V，RUPP M. Lower limb amputation rates in Germany［J］. Medicina，2022，58（1）：101. DOI：10.3390/medicina58010101.

［38］LOCKHART P B，BOLGER A F，PAPAPANOU P N，et al. Periodontal disease and atherosclerotic vascular disease：does the evidence support an independent association? ：a scientific statement from the American Heart

chinaXiv:202310.03350v1

Association［J］. Circulation，2012，125（20）：2520-2544. DOI：10.1161/CIR.0b013e31825719f3.

［39］RUDOLF H，KREUTZER J，KLAASSEN-MIELKE R，et al. Socioeconomic factors and the onset of peripheral artery disease in older adults［J］. Vasa，2021，50（5）：341-347. DOI：10.1024/0301-1526/a000961.

［40］MESSIHA D，PETRIKHOVICH O，LORTZ J，et al. Incomerelated peripheral artery disease treatment：a nation-wide analysis from 2009-2018［J］. J Cardiovasc Dev Dis，2022，9（11）：392. DOI：10.3390/jcdd9110392.

［41］ZHAO Q N，WANG C X，GUAN S CJ，et al. Characterization of the prevalence of peripheral arterial disease in people aged 35 years and above in Beijing and analysis of influencing factors［J］. Chinese Journal of Cardiology，2019，47（12）：1000-1004. DOI：10.3760/cma.j.issn.0253? 3758.2019.12.010.

［42］CAI Y，CUI H，FAN L. Prevalence of cardiovascular and cerebrovascular diseases in army old male hypertensive patients in Beijing [J]. Zhongguo Kangfu Lilun Yu Shijian, 2015, 21（11）: 1298-1303.

［43］LI X K，HAN Y，XU D C，et al. Association between ankle brachial index and mortality in patients with peripheral arterial disease［J］. Journal of Tongji University（Medical Science），2015，36（2）：74-80. DOI：10.16118/j.1008-0392.2015.02.017.

［44］XIA C L，XIAO S Q，WU Q J，et al. Association between passive smoking and health among Chinese nurses：a cross-sectional study［J］. Front Public Health，2021，9：741083. DOI：10.3389/fpubh.2021.741083.

［45］SONG C H，LI W，LENG J H，et al. Passive smoking and postpartum depression among Chinese women：a prospective cohort study in Tianjin，China［J］. Women Health，2019，59（3）：281-293. DOI：10.1080/03630242.2018.1478365.

［46］GARDNER A W，PARKER D E，MONTGOMERY P S，et al. Gender and racial differences in endothelial oxidative stress and inflammation in patients with symptomatic peripheral artery disease［J］. J Vasc Surg，2015，61（5）：1249-1257. DOI：10.1016/j.jvs.2014.02.045.

［47］OKOTH K，CHANDAN J S，MARSHALL T，et al. Association between the reproductive health of young women and cardiovascular disease in later life：umbrella review［J］. BMJ，2020，371：m3502. DOI：10.1136/bmj.m3502.

［48］GENCHEVA D G，NIKOLOV F P，UCHIKOVA E H，et al. Hypertension in pregnancy as an early sex-specific risk factor for cardiovascular diseases：evidence and awareness［J］. Folia Med，2022，64（3）：380-387. DOI：10.3897/folmed.64.e64741.

［49］OLIVER-WILLIAMS C，STEVENS D，PAYNE R A，et al. Association between hypertensive disorders of pregnancy and later risk of cardiovascular outcomes［J］. BMC Med，2022，20（1）：19. DOI：10.1186/s12916-

chinaXiv:202310.03350v1

021-02218-8.

［50］LIU W F，YANG C Z，CHEN Z，et al. Global death burden and attributable risk factors of peripheral artery disease by age，sex，SDI regions，and countries from 1990 to 2030：results from the Global Burden of Disease study 2019［J］. Atherosclerosis，2022，347：17-27. DOI：10.1016/j.atherosclerosis.2022.03.002.

chinaXiv:202310.03350v1